REMARKS

Claims 8-12 and 17-28, of which claims 8, 10, 18-19, 23-24, and 27-28 are currently amended, are pending and appear in this application for the Examiner's review and consideration. Claims 8, 19, 24, and 27-28 are amended for clarity, and claims 18 and 23 are amended for consistency. Claim 10 is amended to correct a typographical error. As no new matter is introduced by the amendments, entry of the amendments at this time is respectfully requested.

Applicants acknowledges with appreciation the Examiner's withdrawal of the objection of the claims for depending on non-elected inventions and the rejection of claims 8-11, 12, and 17 under 35 U.S.C. § 112, second paragraph; claims 10-12 under 35 U.S.C. § 112, first paragraph; and claims 8-10 and 12 under 35 U.S.C. § 102(b).

Claims 18 and 23 are objected to for inconsistency. In response, these claims are amended to recite "mAb 240, mAb 246 and mAb 421" as the Examiner suggested, and the objection should be withdrawn.

Claims 8-12, 17, and 18-28 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement for the reasons set forth on page 4 of the Office Action. Claim 8 is herein amended to recite that the claimed synthetic peptide is 7 to 30 amino acid residues in length of a variable region of an anti-p53 mAb and contains a sequence of a CDR of heavy or light chain of the anti-p53 mAb. The amendment thus clarifies that the claimed synthetic peptide contains fragments of CDR sequences and optional flanking amino acids from an anti-p53 mAb. Applicants respectfully submit that the specification provides sufficient disclosure such that one skilled in the art would reasonably conclude that Applicants had possession of the presently claimed invention at the time the application was filed (*see, e.g.*, Examples, which demonstrate preparation of CDR-based peptides of anti-p53 mAbs and their use for inducing anti-p53 immunity). Accordingly, this rejection should be withdrawn.

Claims 8-9, 17, 18-21, and 27-28 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons stated on pages 4-5 of the Office Action. In the interest of expediting the prosecution of this application, and not as concession to the rejection, claims 8 and 27-28 are amended to delete the recitation "chemical derivatives." Claims 19 and 24 are amended to change "based on" to "containing." As such, the specification provides sufficient direction and guidance to enable a person of ordinary skill in the art to practice the claimed invention without

undue experimentation. For example, a skilled artisan would reasonably expect, based on the present disclosure, that a CDR peptide derived from an anti-p53 mAb that is capable of eliciting anti-p53 Abs would also generate anti-p53 Abs in an animal. Hence, a skilled artisan would have a reasonable expectation that peptides with 7 to 30 amino acids of the variable region of an anti-p53 mAb containing such CDR sequence would also produce such Abs in an animal.

Accordingly, Applicants respectfully request that all rejections under 35 U.S.C. § 112, first paragraph, be withdrawn.

Claims 19 and 24 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for reciting "based on." Amended claims 19 and 24 recite "containing" instead of "based on," and this rejection should therefore be withdrawn.

Claims 8-9, 17, 20, 27-28 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Zusman *et al.* (*The Cancer Journal* 10:116-120 (1997)) and further in view of U.S. Patent No. 5,068,177 (Carson *et al.*) for the reasons stated on pages 7-9 of the Office Action. Applicants respectfully traverse.

While Zusman discloses the tumor suppression effects of an anti-p53 antibody, it does not teach, disclose or suggest immunization with CDR peptides from an anti-p53 Ab to generate an antibody that will achieve the same results.

Likewise, Carson fails to teach, disclose, or suggest a synthetic peptide capable of eliciting antibodies to p53, wherein the peptide is 7 to 30 amino acid residues in length of a variable region of an anti-p53 mAb. Carson relates to production of peptides comprising CDRs of certain Abs collectively termed IgM-RF, and shows that immunization with several such peptides conjugated to a carrier protein elicits production of Abs in an animal. The Abs so produced (Ab2) are capable of binding IgM-RF (Ab1), and can be useful for neutralizing IgM-RF Abs naturally occurring as pathologic autoantibodies in a subject having an autoimmune disease, and for diagnosing the presence of such autoantibodies in a subject. Carson, however, neither teaches, discloses, nor suggests production of anti-anti idiotypic Abs (Ab3) upon immunization with CDR peptides derived from Ab1, or with conjugates of such peptides.

In fact, at the time the present invention was made, an anti-idiotypic network yielding Ab3 was suggested to be produced only by immunization with a complete Ab1 or an immunogen that structurally mimics the binding site of an Ab1. Prior to the present invention, the hypervariable regions constituting the binding site were believed to be "discontinuous at the

level of primary structure but [to] converge at the level of tertiary structure to form the continuous, highly contorted sequence of the binding site" (*see* Carson, at col. 2, lines 20-23). Hence, a person of ordinary skill in the art would not have been motivated, at the time of the present invention, to synthesize short CDR peptides from anti-p53 Abs. Indeed, despite the fact that production of anti-idiotypic Abs (Ab2) by vaccination with CDR peptide conjugates has been publicly known since the 1980s, as described in Carson, and that immunization with whole Abs has shown marked therapeutic disadvantages, it has not been disclosed or suggested to use such peptides as immunogens for inducing Ab3 in a subject, e.g., for inducing anti-tumor immunity.

Carson not only fails to suggest the present synthetic peptide, but it instead teaches away from immunization with unconjugated CDR peptides by disclosing that "the polypeptide alone is not immunogenic in most cases" (col. 4, lines 7-8) and that polypeptides shorter than 35 amino acids in length should therefore be used as peptide-carrier conjugates (col. 4, lines 8-10; col. 13, lines 25-37). The invention disclosed in Carson is exemplified by use of peptide-KLH conjugates rather than unconjugated CDR peptides (*see, e.g.,* col. 41, lines 15-21). Therefore, Carson in fact leads away from the present invention, by discouraging synthesis and use of unconjugated CDR peptides.

Accordingly, neither Zusman nor Carson, alone or in combination, renders the present synthetic peptide obvious, and the 35 U.S.C. § 103(a) rejection based on these references should be withdrawn.

Claims 8-9, 17-21, 23-24, and 27-28 are also rejected under 35 U.S.C. § 103(a) as being unpatentable over Zusman, further in view of Carson and Jannot *et al.* (BBRC 230:242-246 (1997)) for the reasons stated on pages 9-11 of the Office Action. Applicants respectfully traverse.

As explained above, Zusman and Carson do not teach, disclose, or suggest the synthetic peptide of the present claims. Combination of these references with Jannot also does not render the present claims obvious.

Jannot merely discloses single chain Ab ScFv-421, which comprises the variable region sequences, including CDR sequences, of polyclonal Ab PAb-421, and its ability to bind p53. Jannot does not disclose or suggest immunization with this antibody, or a synthetic peptide

derived therefrom, to induce anti-tumor immunity. Further, the reference does not disclose an *isolated* peptide of 7-30 amino acids comprising a CDR sequence of ScFv-421.

Thus, the Examiner appears to be employing an improper hindsight in rejecting the present claims for obviousness based on the cited references. It would not have been obvious to a person having ordinary skill in the art to combine the teachings of Jannot with Zusman, which merely discloses tumor suppression effects of a specific anti-p53 Ab, and Carson, which discloses production of CDR peptide conjugates for eliciting Ab2 production, to achieve the present synthetic peptide. The surprising observation that *isolated, unconjugated CDR peptides* derived from anti-p53 mAbs can generate anti-p53 Abs in an animal was first made in the present application.

Accordingly, Applicants respectfully request that the 35 U.S.C. § 103(a) rejection based on Zusman, Carson, and Jannot be withdrawn.

In view of the above amendments and remarks, the entire application is believed to be in condition for allowance, early notification of such would be appreciated. Should the Examiner not agree, a personal or telephonic interview is respectfully requested to discuss any remaining issues in order to expedite the eventual allowance of the claims.

Respectfully submitted,

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Date

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